10/808,496

# EAST Search History

| Ref # | Hits | Search Query | DBs | Default Operator | Plurals | Time Stamp |
|---|---|---|---|---|---|---|
| L1 | 589 | ((514/217.06) or (514/263.22)).CCLS. | US-PGPUB; USPAT; USOCR | OR | OFF | 2006/12/21 13:34 |
| L2 | 943 | ((544/262) or (544/280)).CCLS. | US-PGPUB; USPAT; USOCR | OR | OFF | 2006/12/21 13:34 |
| L3 | 836 | (546/118).CCLS. | US-PGPUB; USPAT; USOCR | OR | OFF | 2006/12/21 13:34 |
| L4 | 2186 | L1 or L2 or L3 | US-PGPUB; USPAT | OR | OFF | 2006/12/21 13:35 |
| L5 | 19 | L4 and tetrahydro$6naphthyridin$ | US-PGPUB; USPAT | OR | OFF | 2006/12/21 13:35 |

10/ 808,496

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| | | |
|---|---|---|
| NEWS 1 | | Web Page URLs for STN Seminar Schedule - N. America |
| NEWS 2 | | "Ask CAS" for self-help around the clock |
| NEWS 3 | AUG 09 | INSPEC enhanced with 1898-1968 archive |
| NEWS 4 | AUG 28 | ADISCTI Reloaded and Enhanced |
| NEWS 5 | AUG 30 | CA(SM)/CAplus(SM) Austrian patent law changes |
| NEWS 6 | SEP 11 | CA/CAplus enhanced with more pre-1907 records |
| NEWS 7 | SEP 21 | CA/CAplus fields enhanced with simultaneous left and right truncation |
| NEWS 8 | SEP 25 | CA(SM)/CAplus(SM) display of CA Lexicon enhanced |
| NEWS 9 | SEP 25 | CAS REGISTRY(SM) no longer includes Concord 3D coordinates |
| NEWS 10 | SEP 25 | CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine |
| NEWS 11 | SEP 28 | CEABA-VTB classification code fields reloaded with new classification scheme |
| NEWS 12 | OCT 19 | LOGOFF HOLD duration extended to 120 minutes |
| NEWS 13 | OCT 19 | E-mail format enhanced |
| NEWS 14 | OCT 23 | Option to turn off MARPAT highlighting enhancements available |
| NEWS 15 | OCT 23 | CAS Registry Number crossover limit increased to 300,000 in multiple databases |
| NEWS 16 | OCT 23 | The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded |
| NEWS 17 | OCT 30 | CHEMLIST enhanced with new search and display field |
| NEWS 18 | NOV 03 | JAPIO enhanced with IPC 8 features and functionality |
| NEWS 19 | NOV 10 | CA/CAplus F-Term thesaurus enhanced |
| NEWS 20 | NOV 10 | STN Express with Discover! free maintenance release Version 8.01c now available |
| NEWS 21 | NOV 20 | CAS Registry Number crossover limit increased to 300,000 in additional databases |
| NEWS 22 | NOV 20 | CA/CAplus to MARPAT accession number crossover limit increased to 50,000 |
| NEWS 23 | DEC 01 | CAS REGISTRY updated with new ambiguity codes |
| NEWS 24 | DEC 11 | CAS REGISTRY chemical nomenclature enhanced |
| NEWS 25 | DEC 14 | WPIDS/WPINDEX/WPIX manual codes updated |
| NEWS 26 | DEC 14 | GBFULL and FRFULL enhanced with IPC 8 features and functionality |
| NEWS 27 | DEC 18 | CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role |
| NEWS 28 | DEC 18 | CA/CAplus patent kind codes updated |
| NEWS 29 | DEC 18 | MARPAT to CA/CAplus accession number crossover limit increased to 50,000 |
| NEWS 30 | DEC 18 | MEDLINE updated in preparation for 2007 reload |

NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.

```
 NEWS HOURS     STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN     Welcome Banner and News Items
 NEWS IPC8      For general information regarding STN implementation of IPC 8
 NEWS X25       X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FILE 'HOME' ENTERED AT 11:55:57 ON 21 DEC 2006

=> file reg
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 11:56:11 ON 21 DEC 2006
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STRUCTURE FILE UPDATES:   20 DEC 2006  HIGHEST RN 916134-56-0
DICTIONARY FILE UPDATES:  20 DEC 2006  HIGHEST RN 916134-56-0

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TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

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http://www.cas.org/ONLINE/UG/regprops.html

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Uploading C:\Program Files\Stnexp\Queries\10808496s.str
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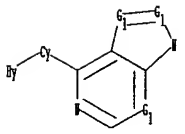
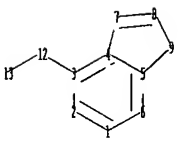




chain nodes :
12 13
ring nodes :
1 2 3 4 5 6 7 8 9
chain bonds :
3-12 12-13
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-9 7-8 8-9
exact/norm bonds :
1-2 1-6 2-3 3-4 3-12 4-5 4-7 5-6 5-9 7-8 8-9 12-13
isolated ring systems :
containing 1 :

G1:C,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 12:Atom
13:Atom
Generic attributes :
12:
Number of Carbon Atoms : less than 7
Type of Ring System : Monocyclic
13:
Number of Carbon Atoms : 7 or more
Number of Hetero Atoms : 2 or more
Type of Ring System : Polycyclic

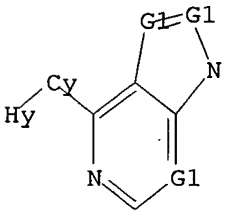
Element Count :
Node 12: Limited
N,N0-1
O,O0
S,S0

10/ 808,496

Node 13: Limited
N,N2
O,O0
S,S0

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR




G1 C,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 61159 TO ITERATE

3.3% PROCESSED 2000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1208444 TO 1237916
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 11:57:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1225814 TO ITERATE

81.6% PROCESSED 1000000 ITERATIONS 14 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.12

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1225814 TO 1225814
PROJECTED ANSWERS: 14 TO 29

L3 14 SEA SSS FUL L1

=> file hcaplus

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 167.38 | 167.59 |

FILE 'HCAPLUS' ENTERED AT 11:57:24 ON 21 DEC 2006
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FILE COVERS 1907 - 21 Dec 2006 VOL 145 ISS 26
FILE LAST UPDATED: 20 Dec 2006 (20061220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 11:55:57 ON 21 DEC 2006)

FILE 'REGISTRY' ENTERED AT 11:56:11 ON 21 DEC 2006
L1 STRUCTURE UPLOADED
L2 0 S L1 SAMPLE
L3 14 S L1 FUL

FILE 'HCAPLUS' ENTERED AT 11:57:24 ON 21 DEC 2006

=> s l3
L4 15 L3

=> d l4 1- ibib abs hitstr
YOU HAVE REQUESTED DATA FROM 15 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1329696 HCAPLUS
DOCUMENT NUMBER: 144:45525
TITLE: Methods for treating mast cell disorders
INVENTOR(S): Hayflick, Joel S.; Pefaur, Noah; Puri, Kamal D.; Tino, William
PATENT ASSIGNEE(S): Icos Corporation, USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|

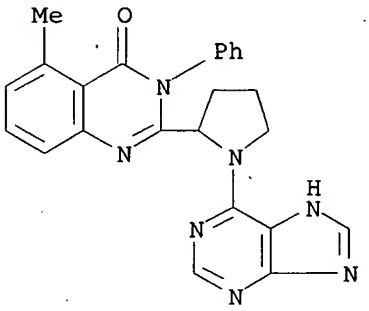
WO 2005120511 A1 20051222 WO 2005-US19558 20050604
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-576947P P 20040604
OTHER SOURCE(S): MARPAT 144:45525

AB The invention provides methods of inhibiting mast cell activity by administering a selective inhibitor of phosphoinositide 3-kinase delta (PI3Kδ). The invention also provides methods for treating or preventing a condition associated with undesirable mast cell activity in an individual comprising administering an effective amount of a selective PI3Kδ inhibitor.

IT 871585-61-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating mast cell disorders)

RN 871585-61-4 HCAPLUS
CN 4(3H)-Quinazolinone, 5-methyl-3-phenyl-2-[1-(1H-purin-6-yl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

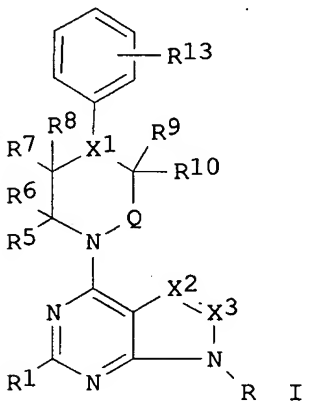
L4 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1314205 HCAPLUS
DOCUMENT NUMBER: 144:51610
TITLE: Preparation and structure activity of pyrazolo-pyrimidine derivatives as antitumor agents and kinase modulators
INVENTOR(S): Anand, Neel K.; Blazey, Charles M.; Bowles, Owen Joseph; Bussenius, Joerg; Canne Bannen, Lynne; Chan, Diva Sze-Ming; Chen, Baili; Co, Erick Wang; Costanzo, Simona; Defina, Steven Charles; Dubenko, Larisa; Franzini, Maurizio; Huang, Ping; Jammalamadaka, Vasu; Khoury, Richard George; Kim, Moon Hwan; Klein, Rhett Ronald; Le, Donna Tra; Mac, Morrison B.; Nuss, John M.; Parks, Jason Jevious; Rice, Kenneth D.; Tsang, Tsze H.; Tsuhako, Amy Lew; Wang, Yong; Xu, Wei

10/ 808,496

PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 211 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005117909 | A2 | 20051215 | WO 2005-US13860 | 20050422 |
| WO 2005117909 | A3 | 20060427 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2005249380 | A1 | 20051215 | AU 2005-249380 | 20050422 |
| CA 2563699 | A1 | 20051215 | CA 2005-2563699 | 20050422 |
| PRIORITY APPLN. INFO.: | | | US 2004-564908P P | 20040423 |
| | | | WO 2005-US13860 W | 20050422 |

OTHER SOURCE(S): MARPAT 144:51610
GI

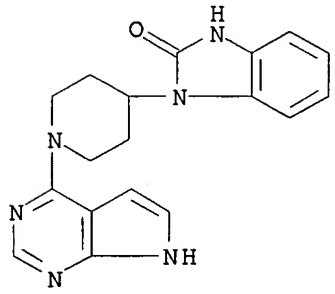



AB Pyrazolo-pyrimidine derivs. I, wherein X1 is N, CR2. X2 is N, CR3; X3 is N, CR4, but when X2 is N then X3 is CR4; R is H, halogen, tri-halomethyl, substituted nitrogen, substituted sulfur, sulfonyl, sulfonamide, carboxylate, amide, substituted oxygen, acyl, alkyl, aryl, heterocycle, heterocycloalkyl, arylalkyl R1-R13 are independently H, halogen, tri-halomethyl, CN, NO2, substituted nitrogen, substituted sulfur, sulfonyl, sulfonamide, carboxylate, amide, substituted oxygen, acyl, alkyl, aryl, heterocycle, heterocycloalkyl, arylalkyl; Q is (C)nR11R12; n is 0-1 are prepared as kinase modulators. Combination chemotherapy and structure activity of title compds. are reported. The compds. modulate

protein kinase enzymic activity to modulate cellular activities such as proliferation, differentiation, programmed cell death, migration and chemoinvasion. Compds. of the invention inhibit, regulate and/or modulate kinases, particularly p70S6 and/or AKT kinases. Methods of using and preparing the compds., and pharmaceutical compns. thereof, to treat kinase-dependent diseases and conditions are also an aspect of the invention. Thus, 3-(azetidin-3-ylidene-methyl)-4-[4-(5-chloro-2-methylphenyl)piperazin-1-yl]-1H-pyrazolo[3,4-d]pyrimidine was prepared and tested in vitro as kinase modulator (IC50 > 1000 nM).

IT 252722-35-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity of pyrazolopyrimidine derivs. as antitumor agents and kinase modulators)

RN 252722-35-3 HCAPLUS
CN 2H-Benzimidazol-2-one, 1,3-dihydro-1-[1-(1H-pyrrolo[2,3-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1259353 HCAPLUS
DOCUMENT NUMBER: 144:22759
TITLE: Preparation of purine quinazolinones as inhibitors of human phosphatidylinositol 3-kinase delta
INVENTOR(S): Fowler, Kerry W.; Huang, Danwen; Kesicki, Edward A.; Ooi, Hua Chee; Oliver, Amy R.; Ruan, Fuqiang; Treiberg, Jennifer
PATENT ASSIGNEE(S): Icos Corporation, USA
SOURCE: PCT Int. Appl., 247 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005113556 | A1 | 20051201 | WO 2005-US16778 | 20050512 |

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2005113554 A2 20051201 WO 2005-US16661 20050512

WO 2005113554 A3 20060406

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-570784P P 20040513

OTHER SOURCE(S): MARPAT 144:22759

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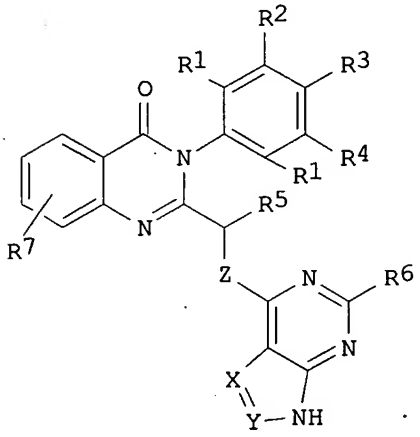


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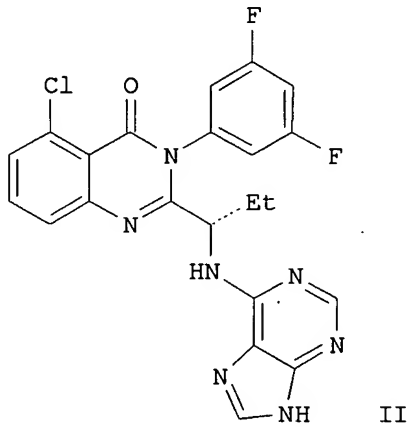



II

AB Quinazolinone derivs. of formula I [X, Y = N, (substituted) CH; Z = NH, O; R1-R3 = H, halo, alkyl; R4 = H, halo, OH, alkoxy, CN, acyl, etc.; R5 = alkyl, Ph, CH2C.tplbond.CH, etc.; R6 = H, halo, (substituted) NH2; R7 = alkyl, halo, CF3, etc.; ZR5 = alkylene] are prepared that inhibit PI3Kδ activity. Methods of inhibiting phosphatidylinositol 3-kinase delta isoform (PI3Kδ) activity, and methods of treating diseases, such as disorders of immunity and inflammation in which PI3Kδ plays a role in leukocyte function, using the compds. also are disclosed. Thus, II was prepared, and had EC50 value of 1.6 nM in human B lymphocyte assay.

IT 870281-11-1P

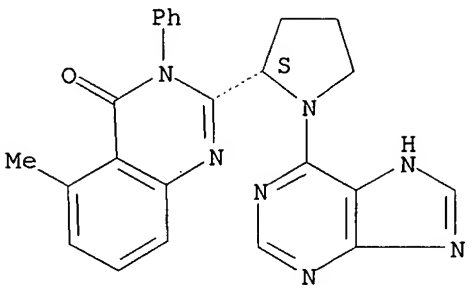
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of purine quinazolinones as inhibitors of human phosphatidylinositol 3-kinase δ)

RN 870281-11-1 HCAPLUS

CN 4(3H)-Quinazolinone, 5-methyl-3-phenyl-2-[(2S)-1-(1H-purin-6-yl)-2-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:232615 HCAPLUS
DOCUMENT NUMBER: 142:291403
TITLE: Use of phosphodiesterase 4 (PDE4) inhibitors for the treatment of diabetes mellitus
INVENTOR(S): Hauser, Daniela; Hanauer, Guido; Grundler, Gerhard; Schmidt, Beate; Kemkowski, Joerg; Kley, Hans-Peter
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005023253 | A1 | 20050317 | WO 2004-EP52005 | 20040902 |
| WO 2005023253 | A8 | 20060302 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004269923 | A2 | 20050317 | AU 2004-269923 | 20040902 |
| AU 2004269923 | A1 | 20050317 | | |
| CA 2537230 | A1 | 20050317 | CA 2004-2537230 | 20040902 |
| US 2006281745 | A1 | 20061214 | US 2006-570622 | 20060303 |

PRIORITY APPLN. INFO.: EP 2003-20126 A 20030905
WO 2004-EP52005 W 20040902

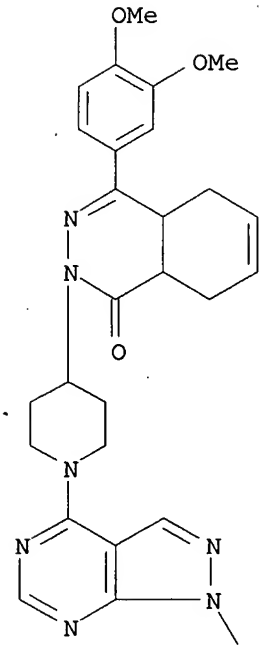
AB The invention discloses the use of certain known PDE4 inhibitors for the treatment of diabetes mellitus and accompanying disorders thereof.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitors for treatment of diabetes mellitus)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1036929 HCAPLUS
DOCUMENT NUMBER: 142:16825
TITLE: Composition comprising a PDE4 inhibitor and a PDE5 inhibitor
INVENTOR(S): Dunkern, Thorsten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein Ardeschir
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004103407 | A2 | 20041202 | WO 2004-EP50869 | 20040519 |
| WO 2004103407 | A3 | 20050217 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,

GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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|---|---|---|---|---|---|
| AU 2004241749 | A1 | 20041202 | AU 2004-241749 | | 20040519 |
| CA 2525946 | A1 | 20041202 | CA 2004-2525946 | | 20040519 |
| EP 1628682 | A2 | 20060301 | EP 2004-766017 | | 20040519 |
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| BR 2004010326 | A | 20060523 | BR 2004-10326 | | 20040519 |
| CN 1791429 | A | 20060621 | CN 2004-80013349 | | 20040519 |
| JP 2006528229 | T | 20061214 | JP 2006-530210 | | 20040519 |
| US 2006094723 | A1 | 20060504 | US 2005-556888 | | 20051115 |
| NO 2005005941 | A | 20051214 | NO 2005-5941 | | 20051214 |
| PRIORITY APPLN. INFO.: | | | EP 2003-11609 | A | 20030522 |
| | | | WO 2004-EP50869 | W | 20040519 |

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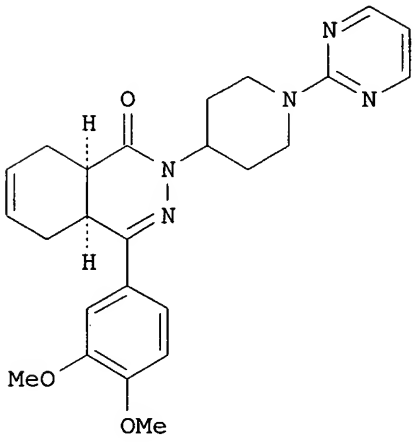



I

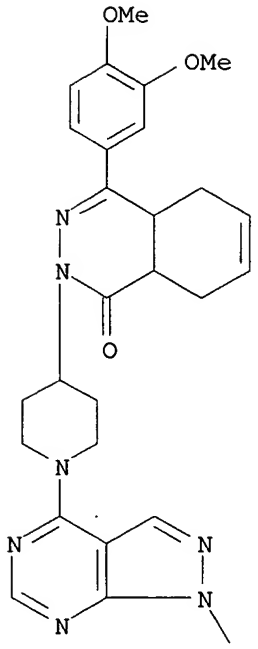
AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is I.

IT 449760-28-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and a PDE5 inhibitor)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


L4 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:996001 HCAPLUS
DOCUMENT NUMBER: 141:406065
TITLE: Composition comprising a PDE-4 inhibitor and a TNF-alpha antagonist
INVENTOR(S): Barsig, Johannes; Weimar, Christian
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098633 | A1 | 20041118 | WO 2004-EP50748 | 20040510 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,

EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10581 A 20030512

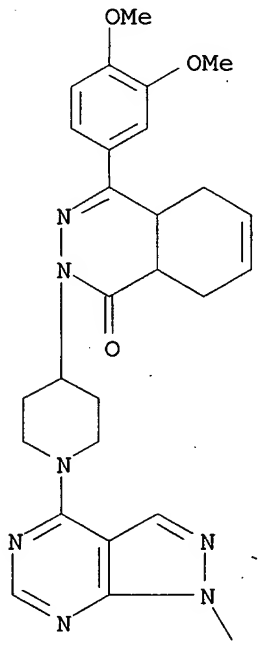
AB The invention relates to the combined administration of a PDE4 inhibitor and a TNFα antagonist selected from the group consisting of etanercept, onercept and pegsunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNFα) activity is detrimental.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic activity of phosphodiesterase 4 inhibitors and TNFα antagonists)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:995979 HCAPLUS

DOCUMENT NUMBER: 141:406064

TITLE: Composition comprising a PDE4 inhibitor and soluble

human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098606 | A1 | 20041118 | WO 2004-EP50749 | 20040510 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

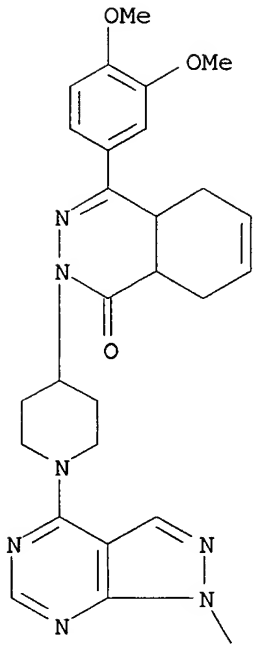
PRIORITY APPLN. INFO.: EP 2003-10596 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and shuIL-1R II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy)

RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:995978 HCAPLUS
DOCUMENT NUMBER: 141:406063
TITLE: Pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098605 | A1 | 20041118 | WO 2004-EP50747 | 20040510 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10631 A 20030512

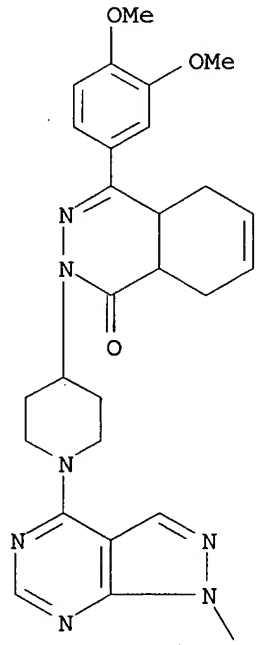
AB The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

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REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:995956 HCAPLUS

DOCUMENT NUMBER: 141:416024

TITLE: Composition comprising a PDE4 inhibitor and a

10/ 808,496

TNFα antagonist
INVENTOR(S): Barsig, Johannes; Weimar, Christian
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004098578 | A2 | 20041118 | WO 2004-EP50750 | 20040510 |
| WO 2004098578 | A3 | 20041229 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

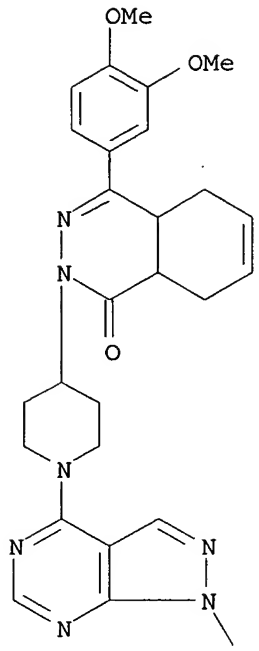
PRIORITY APPLN. INFO.: EP 2003-10593 A 20030512

AB The invention relates to the combined administration of a PDE4 inhibitor and a TNFα antagonist selected from the group consisting of infliximab, adalimumab, cdp870 and cdp571 for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNFα) activity is detrimental.

IT 449760-28-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections containing phosphodiesterase 4 inhibitors in combination with TNFα antagonists for treatment of arthritis and other diseases)

RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


L4 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:610086 HCAPLUS
DOCUMENT NUMBER: 141:134069
TITLE: PDE4 inhibitors for the treatment of neoplasms of lymphoid cells
INVENTOR(S): Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker; Sanders, Karl; Garattini, Enrico; Braunger, Juergen; Schudt, Christian
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004062671 | A2 | 20040729 | WO 2004-EP196 | 20040114 |
| WO 2004062671 | A3 | 20050127 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ | | | | |
| AU 2004204355 | A1 | 20040729 | AU 2004-204355 | 20040114 |

| | | | | |
|---|---|---|---|---|
| CA 2512819 | A1 | 20040729 | CA 2004-2512819 | 20040114 |
| EP 1587512 | A2 | 20051026 | EP 2004-701902 | 20040114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006515367 | T | 20060525 | JP 2006-500561 | 20040114 |
| US 2006148804 | A1 | 20060706 | US 2005-542088 | 20050713 |
| PRIORITY APPLN. INFO.: | | | EP 2003-787 A | 20030114 |
| | | | WO 2004-EP196 W | 20040114 |

OTHER SOURCE(S): MARPAT 141:134069

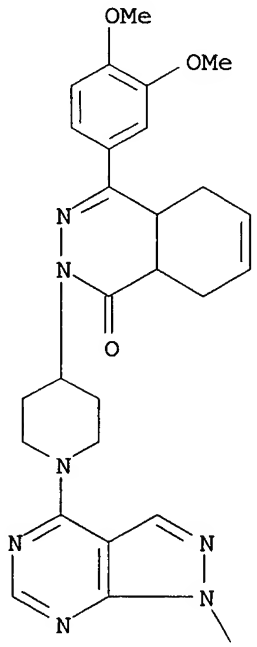
AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concns. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the treatment of neoplasms of lymphoid cells.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

L4 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:719308 HCAPLUS
DOCUMENT NUMBER: 139:240373
TITLE: Pharmaceutical composition of a phosphodiesterase 4 (PDE4) inhibitor or a PDE3/4 inhibitor and a histamine receptor antagonist for the treatment of respiratory diseases
INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-lutz
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003074055 | A1 | 20030912 | WO 2003-EP1876 | 20030225 |
| W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW | | | | |
| RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR | | | | |
| CA 2478612 | A1 | 20030912 | CA 2003-2478612 | 20030225 |
| AU 2003212268 | A1 | 20030916 | AU 2003-212268 | 20030225 |
| EP 1482938 | A1 | 20041208 | EP 2003-708130 | 20030225 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003008220 | A | 20050104 | BR 2003-8220 | 20030225 |
| US 2005112069 | A1 | 20050526 | US 2003-506875 | 20030225 |
| JP 2005524666 | T | 20050818 | JP 2003-572572 | 20030225 |
| NZ 535611 | A | 20060331 | NZ 2003-535611 | 20030225 |
| NO 2004004230 | A | 20041206 | NO 2004-4230 | 20041006 |

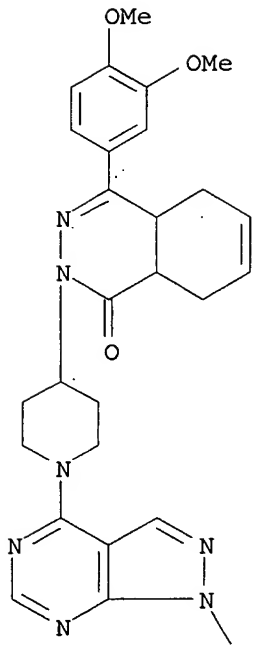
PRIORITY APPLN. INFO.: EP 2002-4987 A 20020306
WO 2003-EP1876 W 20030225

AB The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.

IT 449760-28-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitor or PDE3/4 inhibitor combination with histamine receptor antagonist for treatment of respiratory disease)

RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:637671 HCAPLUS
DOCUMENT NUMBER: 137:185496
TITLE: Preparation of piperidinyl benzopyridazine derivatives as PDE4 inhibitors for treatment of airway disorders
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Kley, Hans-peter; Timmerman, Hendrik; Christiaans, Johannes A. M.; Grundler, Gerhard; Gutterer, Beate; Sterk, Geert Jan
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002064584 | A1 | 20020822 | WO 2002-EP1547 | 20020214 |

W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,

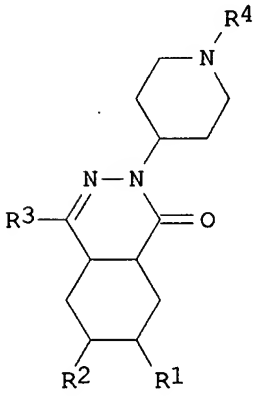
MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

| | | | | |
|---|---|---|---|---|
| CA 2438520 | A1 | 20020822 | CA 2002-2438520 | 20020214 |
| EE 200300311 | A | 20031015 | EE 2003-311 | 20020214 |
| EP 1362044 | A1 | 20031119 | EP 2002-701277 | 20020214 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| HU 200303193 | A2 | 20031229 | HU 2003-3193 | 20020214 |
| BR 2002007278 | A | 20040210 | BR 2002-7278 | 20020214 |
| JP 2004518727 | T | 20040624 | JP 2002-564515 | 20020214 |
| CN 1524080 | A | 20040825 | CN 2002-805038 | 20020214 |
| NZ 527424 | A | 20050225 | NZ 2002-527424 | 20020214 |
| US 2004067946 | A1 | 20040408 | US 2003-467832 | 20030813 |
| US 6953853 | B2 | 20051011 | | |
| NO 2003003618 | A | 20031015 | NO 2003-3618 | 20030814 |
| BG 108124 | A | 20040831 | BG 2003-108124 | 20030821 |
| ZA 2003006815 | A | 20040617 | ZA 2003-6815 | 20030901 |
| US 2005234062 | A1 | 20051020 | US 2005-143721 | 20050603 |

PRIORITY APPLN. INFO.: EP 2001-103496 A 20010215
WO 2002-EP1547 W 20020214
US 2003-467832 A1 20030813

OTHER SOURCE(S): MARPAT 137:185496

GI



I

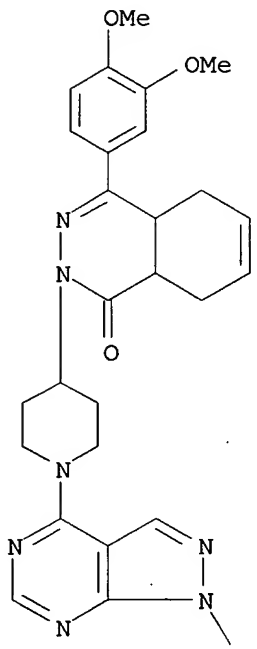
AB Piperidinyl benzopyridazine derivs. [I; wherein R1 and R2 = H, or together form an addnl. bond; R3 = substituted benzene, benzopyran derivative; R4 = (C1-C4)alkoxy, optionally substituted with fluorine] were prepared Thus, to a solution of (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (synthetic preparation given) and p-TsCl in pyridine is stirred to give (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-[1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one. The prepared compds. are effective PDE4 inhibitors useful in the treatment of airway disorders.

IT 449760-28-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for treatment of airway disorders)

RN 449760-28-5 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A




PAGE 2-A

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:171900 HCAPLUS
DOCUMENT NUMBER: 136:216764
TITLE: Process for the preparation of 3-(6-piperidinylpurin-9-yl)propionates as vitronectin receptor antagonists
INVENTOR(S): Peyman, Anuschirwan; Schubert, Gerrit
PATENT ASSIGNEE(S): Aventis Pharma Deutschland GmbH, Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002018384 | A1 | 20020307 | WO 2001-EP9985 | 20010829 |

W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK,

LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PH, PL, RO, SG, SI, SK,
TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| DE 10042655 | A1 | 20020314 | DE 2000-10042655 | 20000831 |
| AU 2001093791 | A5 | 20020313 | AU 2001-93791 | 20010829 |
| EP 1315728 | A1 | 20030604 | EP 2001-974220 | 20010829 |
| EP 1315728 | B1 | 20041027 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

| | | | | |
|---|---|---|---|---|
| JP 2004507544 | T | 20040311 | JP 2002-523899 | 20010829 |
| AT 280769 | T | 20041115 | AT 2001-974220 | 20010829 |
| ES 2232665 | T3 | 20050601 | ES 2001-1974220 | 20010829 |
| US 2004248907 | A1 | 20041209 | US 2003-363450 | 20030401 |
| US 6992187 | B2 | 20060131 | | |

PRIORITY APPLN. INFO.: DE 2000-10042655 A 20000831
WO 2001-EP9985 W 20010829

OTHER SOURCE(S): CASREACT 136:216764; MARPAT 136:216764

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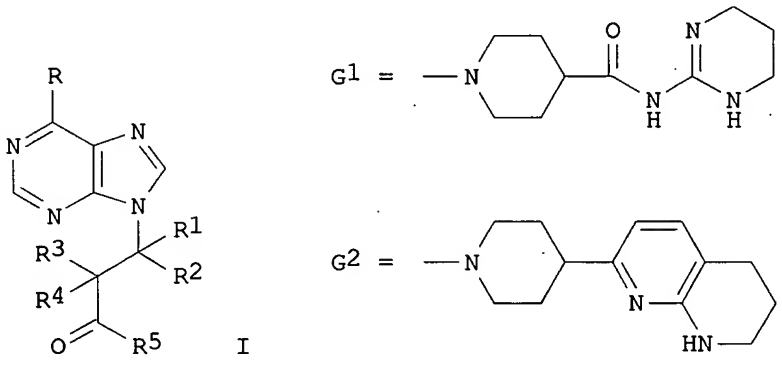


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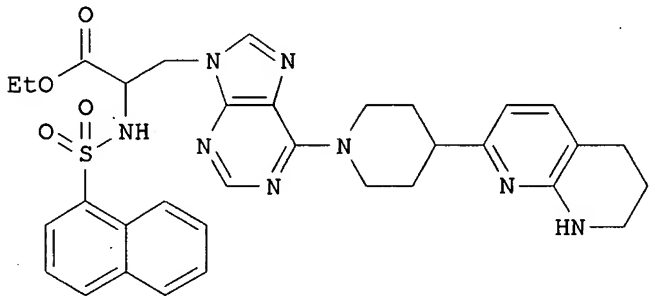


II

AB The present invention relates to a process for the preparation of vitronectin receptor antagonists I [wherein R = G1 or G2; R1, R2, R3, and R4 = independently H, F, Cl, CN, (un)substituted alkyl, cycloalkyl(alkyl), or aryl(alkyl), or R6OR7, R6R6'NR7, R6COR7, R6SO2N(R9)R7, R6OCON(R9)R7, R6CON(R5)R7, R6N(R9)CON(R9)R7, R6N(R9)SO2N(R9)R7, R6SO2R7, R6SCON(R9)R7, R6N(R9)COR7, R6N(R9)SO2R7, R6N(R9)R7, or heterocyclyl; R5 = OH, (aryl)alkoxy, alkylcarbonyloxyalkoxy, or cyclo(alkyl)alkoxy; R6 and R6' = independently (un)substituted alkyl, cycloalkyl(alkyl), aryl(alkyl), or heterocyclyl; R7 = independently alkanediyl or a direct bond; R9 = H or

alkyl; and stereoisomers and salts thereof] by coupling a 9-chloropurine I [R = Cl] to a 4-substituted piperidine and comprises an efficient method for the preparation of I [R = Cl]. In contrast to prior art, the process according to the invention gives good yields in a lower number of steps and can be used advantageously for the syntheses on a relatively large scale. For example, Et (2S)-2-(naphthalene-1-sulfonylamino)-3-aminopropionate was aminated with 4,6-dichloro-5-nitropyrimidine in THF in the presence of TEA and then reduced to the amine using SnCl2 in EtOH. Cyclocondensation with tri-Et orthoformate in N-methylpyrrolidone in the presence of EtSO3H gave the 6-chloropurine. Reaction with 7-(piperidin-4-yl)-1,2,3,4-tetrahydro-[1,8]naphthyridine in DMF and diisopropylethylamine at 70°C for 3 h afforded the piperidinylpurinylpropionate II.

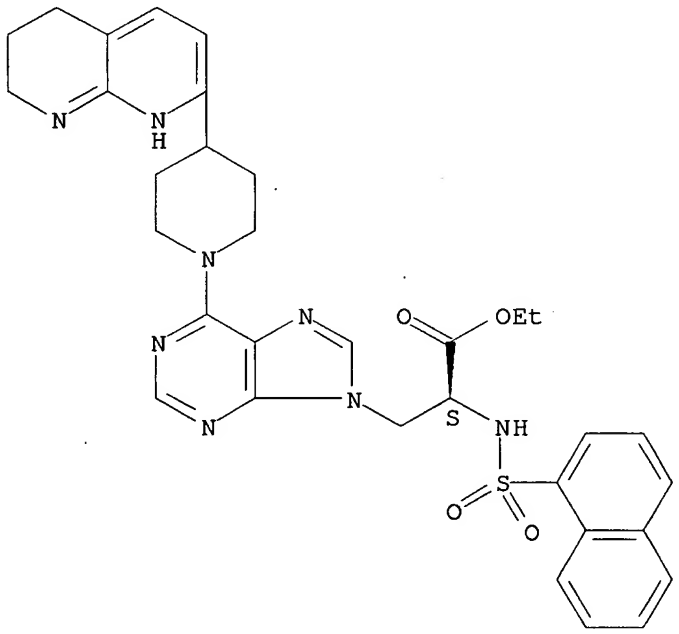
IT 402501-87-5P, Ethyl (2S)-2-(naphthalene-1-sulfonylamino)-3-[6-[4-(5,6,7,8-tetrahydro[1,8]naphthyridin-2-yl)piperidin-1-yl]purin-9-yl]propionate
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(target compound; process for preparation purinylpropionate vitronectin receptor antagonists starting from nitropyrimidines and aminopropionates)

RN 402501-87-5 HCAPLUS

CN 9H-Purine-9-propanoic acid, α-[(1-naphthalenylsulfonyl)amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, ethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A




PAGE 2-A

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:10662 HCAPLUS
DOCUMENT NUMBER: 134:71600
TITLE: Naphthyridine derivatives, processes for their preparation, their use as vitronectin receptor antagonists and inhibitors of cell adhesion, and pharmaceutical compositions comprising them
INVENTOR(S): Peyman, Anuschirwan; Scheunemann, Karl-Heinz; Gourvest, Jean-Francois; Ruxer, Jean-Marie; Gadek, Thomas R.
PATENT ASSIGNEE(S): Aventis Pharma Deutschland G.m.b.H., Germany; Genentech, Inc.
SOURCE: Eur. Pat. Appl., 36 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1065207 | A1 | 20010103 | EP 1999-112636 | 19990702 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| CA 2376668 | A1 | 20010111 | CA 2000-2376668 | 20000626 |
| WO 2001002398 | A1 | 20010111 | WO 2000-EP5920 | 20000626 |
| W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| BR 2000012129 | A | 20020507 | BR 2000-12129 | 20000626 |
| EP 1210348 | A1 | 20020605 | EP 2000-945825 | 20000626 |
| EP 1210348 | B1 | 20050928 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| TR 200103856 | T2 | 20020621 | TR 2001-3856 | 20000626 |
| JP 2003503496 | T | 20030128 | JP 2001-507835 | 20000626 |
| NZ 516058 | A | 20030131 | NZ 2000-516058 | 20000626 |
| HU 200203539 | A2 | 20030228 | HU 2002-3539 | 20000626 |
| EE 200100711 | A | 20030415 | EE 2001-711 | 20000626 |
| AU 775386 | B2 | 20040729 | AU 2000-59787 | 20000626 |
| AT 305471 | T | 20051015 | AT 2000-945825 | 20000626 |
| ES 2250157 | T3 | 20060416 | ES 2000-945825 | 20000626 |
| TW 593319 | B | 20040621 | TW 2000-89117925 | 20000901 |
| BG 106257 | A | 20021031 | BG 2001-106257 | 20011220 |
| HR 2001000946 | A1 | 20030228 | HR 2001-946 | 20011221 |
| NO 2001006404 | A | 20020301 | NO 2001-6404 | 20011228 |
| ZA 2002000016 | A | 20030102 | ZA 2002-16 | 20020102 |
| Parent — US 6743800 | B1 | 20040601 | US 2002-30301 | 20020320 |
| HK 1050003 | A1 | 20050429 | HK 2003-102163 | 20030325 |
| US 2004198718 | A1 | 20041007 | US 2004-808496 | 20040324 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| EP 1999-112636 | A | 19990702 |
| WO 2000-EP5920 | W | 20000626 |
| US 2002-30301 | A3 | 20020320 |

OTHER SOURCE(S): MARPAT 134:71600
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to compds. I. G is -(CR1R2)n-A-(CR1R2)m-(CR1R3)i-(CR1R2)q-R4. A is a direct bond, -C(O)NR5-, -NR5C(O)-, -C(O)-, -NR5-, -O-, -S-, -S(O)-, -S(O)2-, (C2-C4)alkynediyl, (C2-C4)alkenediyl, (C5-C14)arylene where in the arylene residue 1-5 ring C atoms can be replaced by heteroatoms N, O and S, or a divalent residue of a 3-7-membered saturated or unsatd. ring which can contain 1-2 ring heteroatoms N, S and O and which can be monosubstituted or disubstituted by residues :O, :S and R3. B is (C1-C18)alkyl, (C3-C14)cycloalkyl, (C3-C14)cycloalkyl(C1-C8)alkyl, (C5-C14)aryl, (C5-C14)aryl(C1-C8)alkyl, (C5-C14)heteroaryl, (C5-C14)heteroaryl(C1-C8)alkyl, F, Cl, Br, OH, CN, CF3, NO2, CO2H, (C1-C6)alkoxy, (C1-C6)alkoxy(C1-C6)alkyl, (C1-C6)alkoxycarbonyl, (C1-C6)alkylcarbonyl, (C5-C14)arylcarbonyl, (C1-C6)alkylaminocarbonyl, (C1-C6)alkoxy(C1-C6)alkoxy, (C5-C14)aryl(C1-C8)alkylcarbonyl, (C1-C6)alkanoylamino, (C1-C6)alkylsulfonylamino, (C5-C14)arylsulfonylamino, (C1-C6)alkylamino, di((C1-C6)alkyl)amino, (C1-C6)alkylsulfonyl, aminosulfonyl, (C5-C14)arylsulfonyl, (C5-C14)aryl(C1-C8)alkylsulfonyl, (C5-C14)aryl or (C5-C14)heteroaryl, where all residues B are independent of one another and can be identical or different. X is H, NR6R6', F, Cl, Br, OR6, SR6, hydroxy(C1-C6)alkyl-NH-, (hydroxy(C1-C6)alkyl)2N-, amino(C1-C6)alkyl-NH-, (amino(C1-C6)alkyl)2N-, hydroxy(C1-C6)alkyl-O-, hydroxy(C1-C6)alkyl-S- or -NH-C(O)-R6. Y is R5, F, Cl, Br, CN, NR6R6', OR6, SR6 or hydroxy(C1-C6)alkyl-NH-. Z is N or CH. R1 and R2 are H, F, Cl, CN, NO2, (C1-C10)alkyl, (C3-C14)cycloalkyl, (C3-C14)cycloalkyl(C1-C8)alkyl, (C5-C14)aryl, (C5-C14)aryl(C1-C8)alkyl, (C5-C14)heteroaryl, (C5-C14)heteroaryl(C1-C8)alkyl, R6-O-R7, R6-S(O)p-R7, R6S(O)2NHR7, R6OC(O)NHR7 or R6R6'N-R7, where all residues R1 and R2 are independent of one another and can be identical or different. R3 is H, F, Cl, CN, NO2, (C1-C18)alkyl, (C3-C14)cycloalkyl, (C3-C14)cycloalkyl(C1-C8)alkyl, (C5-C14)aryl, (C5-C14)aryl(C1-C8)alkyl, (C5-C14)heteroaryl, (C5-C14)heteroaryl(C1-C8)alkyl, R6-O-R7, R6R6'N-R7, R6C(O)-O-R7, R6C(O)R7, R6OC(O)R7, R6N(R6')C(O)OR7, R6S(O)pN(R5)R7, R6OC(O)N(R5)R7, R6C(O)N(R5)R7, R6N(R6')C(O)N(R5)R7, R6N(R6')S(O)pN(R5)R7, R6S(O)pR7, R6SC(O)N(R5)R7, R6N(R6')C(O)R7 or R6N(R6')S(O)pR7, where alkyl can be monounsatd. or polyunsatd. and where alkyl, cycloalkyl, aryl, and heteroaryl can be monosubstituted or polysubstituted by R6, F, Cl, Br, CN, CF3, R6R6'NR7, NO2, R6OC(O)R7, R6C(O)R7, R6N(R6')C(O)R7, R6N(R6')S(O)pR7 or R6-O-R7, and where all residues R3 are independent of one another and can be identical or different. R4 is -C(O)R8, -C(S)R8, -S(O)pR8, -P(O)R8R8' or a residue of a 4-8-membered saturated or unsatd. heterocycle which contains 1-4 heteroatoms N, O and S. R5 is H, (C1-C10)alkyl, (C3-C14)cycloalkyl, (C3-C14)cycloalkyl(C1-C8)alkyl, (C5-C14)aryl or (C5-C14)aryl(C1-C8)alkyl, where all residues R5 are independent of one another and can be identical or different. R6 and R6' are H, (C1-C18)alkyl, (C3-C14)cycloalkyl, (C3-C14)cycloalkyl(C1-C8)alkyl, (C5-C14)aryl, (C5-C14)aryl(C1-C8)alkyl, (C5-C14)heteroaryl or (C5-C14)heteroaryl(C1-C8)alkyl where aryl, heteroaryl, cycloalkyl and alkyl can be substituted 1-3 times by identical or different substituents F, Cl, Br, CN, CF3, NO2, CO2H, (C1-C6)alkyl, (C1-C6)alkoxy, (C1-C6)alkoxy(C1-C6)alkyl, (C1-C6)alkoxycarbonyl, (C1-C6)alkylcarbonyl, (C1-C6)alkylaminocarbonyl, (C1-C6)alkoxy(C1-C6)alkoxy, (C5-C14)arylcarbonyl, (C5-C14)aryl(C1-C8)alkylcarbonyl, (C1-C6)alkanoylamino, (C5-C14)arylsulfonylamino, (C1-C6)alkylsulfonylamino, (C1-C6)alkylamino, di((C1-C6)alkyl)amino, (C1-C6)alkylsulfonyl, (C1-C6)alkylaminosulfonyl, (C5-C14)arylaminosulfonyl, (C5-C14)aryl(C1-C8)alkylaminosulfonyl, (C5-C14)arylsulfonyl, (C5-C14)aryl(C1-C8)alkylsulfonyl, (C5-C14)aryl and (C5-C14)heteroaryl, and where all residues R6 and R6' are independent of one another and can be identical or different. R7 is (C1-C4)alkanediyl or

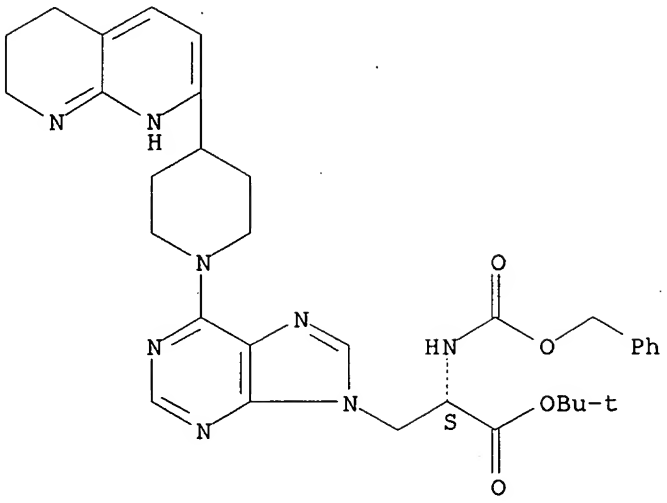
a direct bond, where all residues R7 are independent of one another and can be identical or different. R8 and R8' are OH, (C1-C8)alkoxy, (C5-C14)aryl(C1-C8)alkoxy, (C5-C14)aryloxy, (C1-C8)alkylcarbonyloxy(C1-C4)alkoxy, (C5-C14)aryl(C1-C8)alkylcarbonyloxy(C1-C8)alkoxy, NR6R6', (di((C1-C8)alkyl) amino)carbonylmethyloxy, (di((C5-C14)aryl(C1-C8)alkyl)amino)carbonylmethyloxy, (C5-C14)arylamino, the residue of an amino acid, N-((C1-C4)alkyl)piperidin-4-yloxy, 2-methylsulfonylethoxy, 1,3-thiazol-2-ylmethyloxy, 3-pyridylmethyloxy, 2-(di((C1-C4)alkyl)amino)ethoxy or the residue Q-(CH3)3N+-CH2-CH2-O- in which Q- is a physiol. tolerable anion, where all residues R8 and R8' are independent of one another and can be identical or different. N is 0-5; m is 0-5; i is 0-1; q is 0-2; r is 0-2; s is 0-3; t is 0-8; p is 0-2, where all nos. p are independent of one another and can be identical or different. The claimed compds. also include stereoisomeric forms and mixts. thereof in all ratios, and their physiol. tolerable salts and their prodrugs; where, instead of the purine structure shown I, also a 3-deazapurine structure, a 7-deazapurine structure or a 7-deaza-8-azapurine structure can be present. I are valuable pharmacol. active compds. They are vitronectin receptor antagonists and inhibitors of cell adhesion and are suitable for the therapy and prophylaxis of illnesses which are based on the interaction between vitronectin receptors and their ligands in cell-cell or cell-matrix interaction processes or which can be prevented, alleviated or cured by influencing such interactions. For example, they can be applied for inhibiting bone resorption by osteoclasts and thus for treating and preventing osteoporosis, or for inhibiting undesired angiogenesis or proliferation of cells of the vascular smooth musculature. The invention furthermore relates to processes for the preparation of I, their use, in particular as active ingredients in pharmaceuticals, and pharmaceutical compns. comprising them. The process of preparation comprises reacting II (L1 = leaving group) with III or IV; B, G, X, Y, r, s and t are defined as above but wherein functional groups can also be present in the form of precursor groups or in protected form. For example, (2S)-2-benzyloxycarbonylamino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid tert-Bu ester could be made from 7-(piperidin-4-yl)-1,2,3,4-tetrahydro-1,8-naphthyridine and (S)-2-benzyloxycarbonylamino-3-(6-chloropurin-9-yl)propionic acid tert-Bu ester in DMF in the presence of NEtiPr2; the ester was then hydrolyzed by CF3CO2H to give the desired compound

IT 315240-30-3P, (2S)-2-Benzyloxycarbonylamino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid tert-butyl ester 315240-32-5P, (2S)-2-Amino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid tert-butyl ester 315240-34-7P, (2S)-2-Benzenesulfonylamino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid tert-butyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; naphthyridine derivs., processes for preparation, uses as vitronectin receptor antagonists and inhibitors of cell adhesion, and pharmaceutical compns. comprising them)

RN 315240-30-3 HCAPLUS

CN 9H-Purine-9-propanoic acid, α-[[(phenylmethoxy)carbonyl]amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, 1,1-dimethylethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315240-32-5 HCAPLUS
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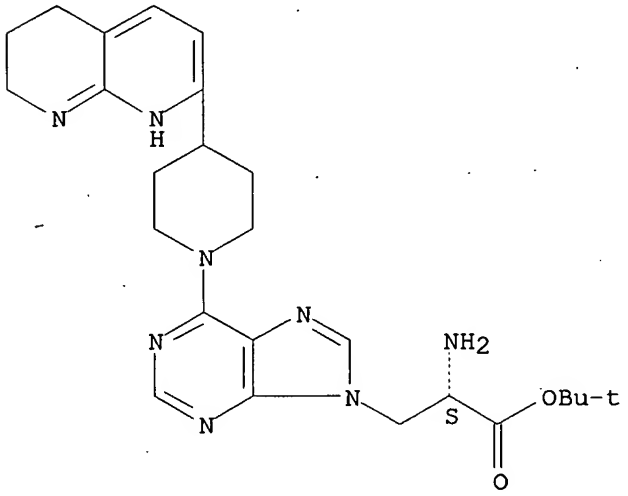
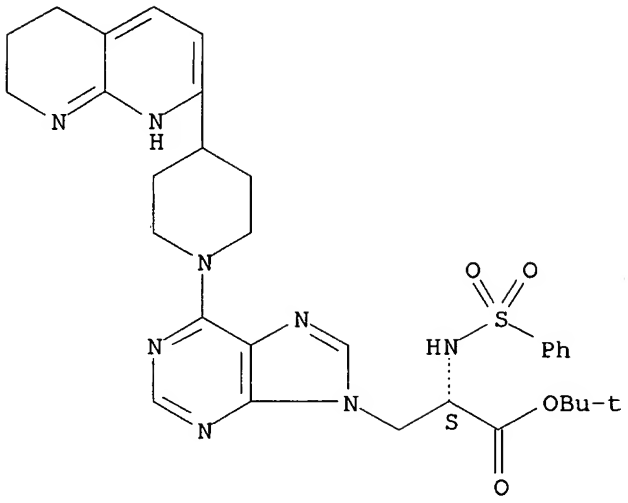
Absolute stereochemistry.



RN 315240-34-7 HCAPLUS
CN 9H-Purine-9-propanoic acid, α-[(phenylsulfonyl)amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, 1,1-dimethylethyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

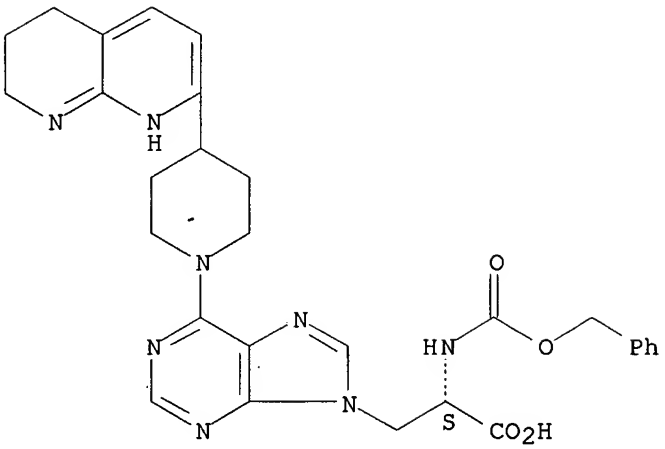


IT 315240-14-3P, (2S)-2-Benzyloxycarbonylamino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid 315240-16-5P, (2S)-2-Benzenesulfonylamino-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid 315240-18-7P, (2S)-2-(4-Chlorobenzenesulfonylamino)-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid 315240-20-1P, (2S)-2-(Naphthalene-1-sulfonylamino)-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid 315240-22-3P, (2S)-3-(6-(4-(5,6,7,8-Tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)-2-(4-trifluoromethylbenzenesulfonylamino)propionic acid 315240-24-5P, (2S)-2-(Butane-1-sulfonylamino)-3-(6-(4-(5,6,7,8-tetrahydro-1,8-naphthyridin-2-yl)piperidin-1-yl)purin-9-yl)propionic acid
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(naphthyridine derivs., processes for preparation, uses as vitronectin receptor antagonists and inhibitors of cell adhesion, and pharmaceutical compns. comprising them)

RN 315240-14-3 HCAPLUS

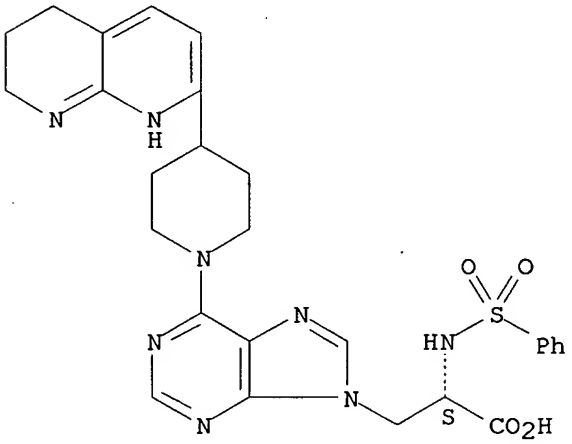
CN 9H-Purine-9-propanoic acid, α-[[(phenylmethoxy)carbonyl]amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, (αS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



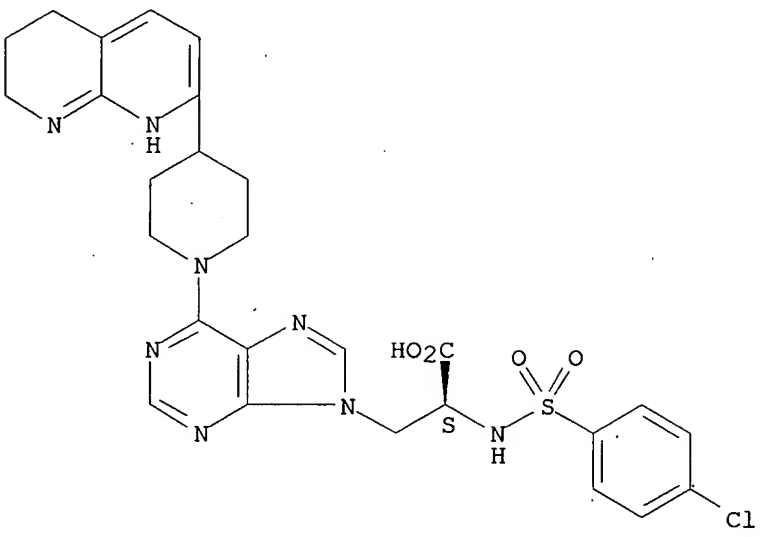
RN 315240-16-5 HCAPLUS
CN 9H-Purine-9-propanoic acid, α-[(phenylsulfonyl)amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



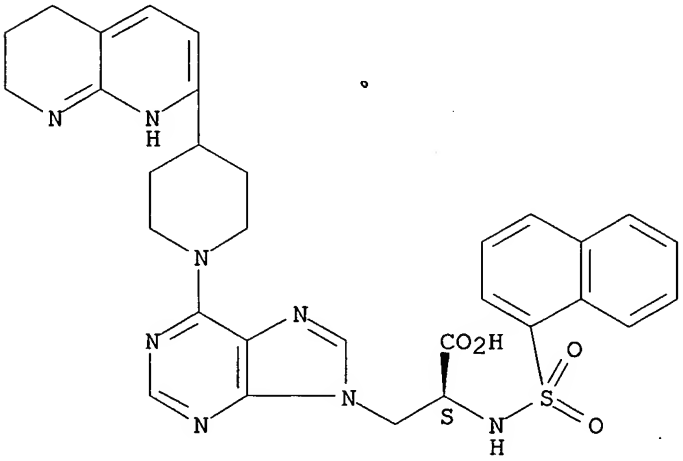
RN 315240-18-7 HCAPLUS
CN 9H-Purine-9-propanoic acid, α-[[(4-chlorophenyl)sulfonyl]amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



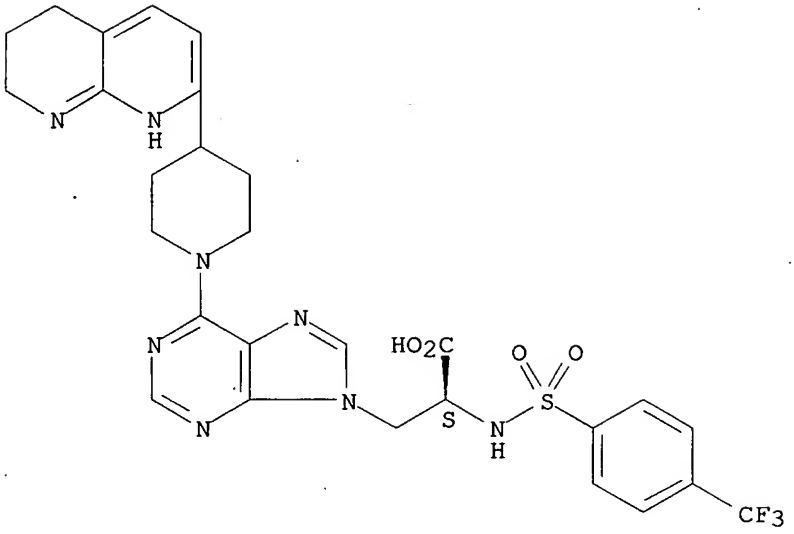
RN 315240-20-1 HCAPLUS
CN 9H-Purine-9-propanoic acid, α-[(1-naphthalenylsulfonyl)amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



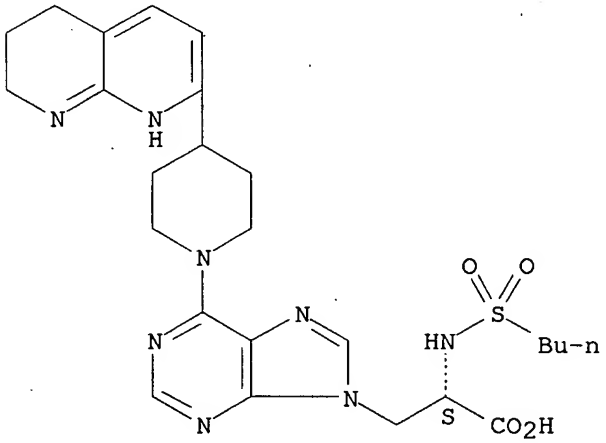
RN 315240-22-3 HCAPLUS
CN 9H-Purine-9-propanoic acid, 6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-α-[[[4-(trifluoromethyl)phenyl]sulfonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 315240-24-5 HCAPLUS
CN 9H-Purine-9-propanoic acid, α-[(butylsulfonyl)amino]-6-[4-(1,5,6,7-tetrahydro-1,8-naphthyridin-2-yl)-1-piperidinyl]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:811245 HCAPLUS
DOCUMENT NUMBER: 132:49976
TITLE: Preparation of pyrrolo[2,3-d]pyrimidines as inhibitors of protein tyrosine kinases such as Janus Kinase 3
INVENTOR(S): Blumenkopf, Todd Andrew; Flanagan, Mark Edward; Brown, Matthew Frank; Changelian, Paul Steven
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9965909 | A1 | 19991223 | WO 1999-IB1110 | | 19990614 |
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| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2335186 | A1 | 19991223 | CA 1999-2335186 | | 19990614 |
| CA 2335186 | C | 20050329 | | | |
| AU 9940545 | A | 20000105 | AU 1999-40545 | | 19990614 |
| AU 758427 | B2 | 20030320 | | | |
| TR 200003720 | T2 | 20010321 | TR 2000-200003720 | | 19990614 |
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| EP 1087971 | B1 | 20040707 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | | |
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| ZA 9904003 | A | 20001218 | ZA 1999-4003 | | 19990617 |
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| W: BW, GH, GM, KE, MW, SD, UG, ZM, ZW | | | | | |
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| NO 2005000201 | A | 20010215 | NO 2005-201 | | 20050113 |
| PRIORITY APPLN. INFO.: | | | US 1998-89886P | P | 19980619 |
| | | | WO 1999-IB1110 | W | 19990614 |
| | | | US 1999-335030 | A1 | 19990617 |

OTHER SOURCE(S): MARPAT 132:49976
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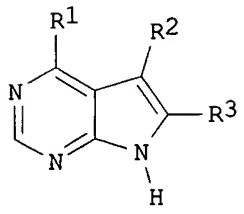

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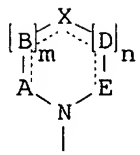


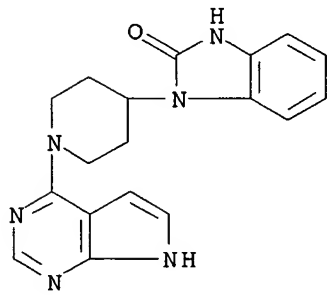
II

AB The title compds. [I; R1 = II (wherein the dashed line represents optional double bonds; m = 0-3; n = 0-3; X, B, D = O, S(O)d (d = 0-2), NR6, CR7R8; A, E = CR7R8; R6 = H, alkyl, CF3, etc.; R7, R8 = H, 2H, alkyl, etc.); R2, R3 = H, NH2, halo, etc.] which are inhibitors of protein tyrosine kinases such as Janus Kinase 3 (no data) and as such useful as immunosuppressive agents for organ transplants, lupus, multiple sclerosis, rheumatoid arthritis, psoriasis, Type I diabetes and complications from diabetes, cancer, asthma, atopic dermatitis, autoimmune thyroid disorders, ulcerative colitis, Crohn's disease, Alzheimer's disease, leukemia and other autoimmune diseases, were prepared E.g., a 2-step synthesis of I [R1 = piperidino; R2 = Cl; R3 = H], starting with 4-chloro-7H-pyrrolo[2,3-d]pyrimidine, was given. Compds. I are effective at 0.1-1000 mg/day.

IT 252722-35-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolo[2,3-d]pyrimidines as inhibitors of protein tyrosine kinases such as Janus Kinase 3)

RN 252722-35-3 HCAPLUS

CN 2H-Benzimidazol-2-one, 1,3-dihydro-1-[1-(1H-pyrrolo[2,3-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 11:56:11 ON 21 DEC 2006
L1 STRUCTURE UPLOADED
L2 0 S L1 SAMPLE
L3 14 S L1 FUL

FILE 'HCAPLUS' ENTERED AT 11:57:24 ON 21 DEC 2006
L4 15 S L3

10/ 808,496

=> log y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 79.18 | 246.77 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -11.25 | -11.25 |

STN INTERNATIONAL LOGOFF AT 11:58:05 ON 21 DEC 2006